From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/051308	30.06.2004	30.06.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/4745, A61P25/00, A61P35/00

Applicant
ALTANA PHARMA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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PCT/ISA/237

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-12 and 14

because:

☒ the said international application, or the said claims Nos. 1-9 and 14 with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 10-12

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	10-12 and 15
	No:	Claims	1-9 and 14 (see separate sheet)

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

III.1 Claims 1-9 and 14 relate to subject-matter considered by this authority to be covered by the provisions of Rule 67.1(iv)PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I)PCT).

III.2 The formulation "as disclosed in WO0248144, WO03014115, WO03014116 or WO03014117 or analogously or similarly thereto" (referring to claims 10-12) violates the requirements of Article 6 PCT. These references to other documents cannot be regarded as technical features. The technical features concerned should be incorporated from the description into the claims.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The applicant's attention is drawn to the fact that the present opinion expressed as to novelty, inventive step and industrial applicability refers only to matter for which an international search report has been drawn up (see section III.1).

V.1 Article 33(4) PCT

The subject-matter of claims 1-9 and 14 involves compositions or substances in a method of treatment of the human/animal body. For the assessment of these claims on the question whether they are industrially applicable, no unitary criteria exist in the PCT Contracting states. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognise the subject-matter of claims related to the use of a compound in medical treatment as industrially applicable. However, the EPO may allow claims related to a known compound in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

V.2. The following documents are referred to in this communication:

D1: WO 03 014116 A (ERGUEDEN JENS-KERIM ;FLUBACHER DIETMAR (DE); STOLTEFUSS JURGEN (DE) 20 February 2003 (2003-02-20)

D2: WO 02 48144 A (ERGUEDEN JENS-KERIM ;FLUBACHER DIETMAR (DE); NIEWOEHNER ULRICH (DE) 20 June 2002 (2002-06-20)

D3: WO 03 051877 A (PERNERSTORFER JOSEF ;BAYER AG (DE); BURKHARDT NILS (DE); NIEWOEHNE) 26 June 2003 (2003-06-26)

V.3 Article 33(3) PCT

D1 (page 1, paragraph 2; claim 4, examples 1-92) and, similarly, D2 (page 1, paragraph 1; claims 1-4; examples 1-91) and D3 (page 1, paragraph 1; claim 1-6, examples 1-440) disclose substituted pyrrolo-isoquinolines with a structure differing from compounds of the present application

- in that they fall under the provisos of claims 1, 2 with R5 being hydrogen or
- in that R5 is different from hydrogen (claims 3, 4, 6) and/or R8 is cyano (claims 3, 4, 8) or
- in that R2 is a halogen atom (several compounds in claim 7).

The PDE10 inhibitory activity of these compounds is also disclosed.

The problem underlying the current application can thus be formulated as providing alternative compounds with PDE10 inhibitory activity (which can e.g. be used to treat cancer). A skilled medicinal chemist would inevitably try to modify the substituents on the basic pyrrolo-isoquinoline structure and use these compounds as PDE10 inhibitors. Thus, there is no inventive step in the sense of Article 33(3) PCT present in the application over D1-D3.